Supplementary materials

Materials and methods

Target proteins

Two sources of proteins were used in the study. One source was purchased from the commercialization approach, including human angiotensin I converting enzyme 2 (ACE-2) (Mammalian, C-6 His, Cat. C419), human Cathepsin B (CTSB) (from HEK293, Mammalian, C-6His, Cat.C398), human Basigin (CD147) (Mammalian, Cat. C433), Human AXL (Mammalian, C-6His, Cat.C02B). SARS-CoV-2 Nucleocapsid Protein (N protein) (*E. coli*, N-6His, Cat. DRA31), non-structural protein 2 of SARS-CoV-2 (NSP2) (*E. coli*, C-6His, CR82), SARS-CoV-2 3C-like Proteinase (3CLpro, *E. coli*, N-6His, CR76), purchased from novoprotein (Shanghai, China); The other proteins were over-expressed in *E. coli* from the laboratory, the human annexin a2, high mobility group protein 1 (HMGB1), nuclear factor kappa B subunit 1 (NFkB1-P50), mitogen-activated protein kinase 1 (MAPK1), TGF-beta activated kinase 1 (TAB1) genes were inserted into the Pet-28a vector with His-tag. Bacteria were lysed by ultrasound and proteins purified by nickel column. All proteins were under unified quality control, which was carried out by gel electrophoresis.

The reasons of target proteins for selection are as follows: ACE-2, CD147, AXL are the main receptors of the virus[1]; Host cell protease CTSB is the key element of the lysosomal pathway, and almost all of them are in lysosomes[2]. 3C-like Proteinase is main proteases of SARS-CoV-2[3]. NSP2 is involved in RNA transcription and replication. NFκB1-P50, anneixn a2, MAPK1, TAB1 and HMGB1 are important

inflammatory regulators [4] [5] [6] [7].

Chip preparation

Protein Thermal Shift Assay was used PCR based automated method with Special Dye from Applied biosystems (California, USA). Taking NFκB1-P50 protein as an example, we analyzed the protein concentration range for detection, and used it as a reference concentration to test other proteins. Finally, we determined that the mass of reactive protein per well was 0.045 μg/μL reaction solution. PBS buffer (pH=7.4, 0.01 M phosphate buffer, 0.0027 M KCl and 0.137 M NaCl), PBS buffer with disaccharide (1% trehalose, trying to increase protein stability by adding disaccharide), PBS buffer with 1% trehalose and 0.1% bacteriostatic agent (5-chloro-2-methyl-4-isothiazolin-3-one2-methyl-4-isothiazloin-3-one, 3:1), and PBS buffer with 0.02% NaN_3 was tested as reaction buffer, with 3CLpro protein (0.15 μg/μL). The universal PCR 96 well plate (Cellpro, Suzhou City, China) was used as the substrate, which will greatly reduce the cost and increase the universality of the chip. Universal fluorescence quantitative PCR instrument (Rocgen, Beijing, China) and Step one plus (Applied biosystems, California, USA) with 20 μL volume was used in this method, select fluorophore reporter as ROX or VIC, none quencher, and the thermal profile 25 ℃- 95 ℃, ramp rate: 0.1 ℃/S, ramp mode: continuous.

Chip application test

We used targeted small molecules and macromolecular drugs to test the application of the chip. Chlorogenic acid (20 μM) (ChemFaces, Wuhan, China) as known annexin a2 binding molecule was selected as a representative of active

natural products to verify the function of the chip. The antibody against N protein (1 μg/well, novoprotein, Shanghai, Beijing) of SARS-CoV-2 was used as a representative of macromolecular to test the application of the chip in the macromolecular field. All experimental conditions were consistent with those described in the above part.

Extraction of plant components

The effective substances of *Pinellia Ternate* were extracted by H_2O extraction (0.076 g/mL). Before the experiment, the herbal extracted solution was treated by ultrafiltration (3 kDa) to remove macromolecules from the mixed system. Because the background signal from macromolecules can affect the detection signal of target protein. After removing macromolecules, the mixture was concentrated in low temperature and vacuum. The concentrated mix (1:10 V/V) was used for thermal stability test, and the dosage of each reaction was 1 μL.

Statistics

The data of protein stability curve were derived from PCR instrument. Then, the curve is drawn by software (Office Excel, Microsoft), and the highest point of fluorescence signal is taken as Tm value. Difference in Tm value statistical significance was set at $P<0.05$, and *t* test used.

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